RESEARCH HIGHLIGHTS

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cisplatin and 5-FU, and 52 with paclitaxelbased regimens. The pathologic complete response rates for paclitaxel-containing regimens and non-paclitaxel-containing regimens were 39% and 40%, respectively (P=0.90). As expected, the paclitaxel-containing regimens comprising three drugs led to more toxicity than the two-drug combination of cispatin and 5-FU (grade 3–4 toxicity 41% vs 24%).

The authors note that the analysis had limitations, and variations in treatments and surgical technique may have affected the outcome. They suggest that further studies testing targeted agents in combination with radiation therapy are needed.

Original article Kelsey CR *et al.* (2007) Paclitaxel-based chemoradiotherapy in the treatment of patients with operable esophageal cancer. *Int J Radiat Oncol Biol Phys* **69:** 770–776

Radiotherapy and hormone therapy in patients with high-risk prostate cancer

Standard treatment of localized intermediate and/or high-risk prostate cancer comprises external-beam radiotherapy and hormonal therapy. This combination improves overall survival, but there is still some controversy surrounding the value of pelvic lymph node irradiation, as well as the timing of androgen suppression. The Radiation Therapy Oncology Group (RTOG) study 94-13 was designed to investigate whether whole pelvic radiotherapy (WPRT) is better than prostate-only radiotherapy (PORT) for high-risk disease and how neoadjuvant hormone therapy (NHT) compared with adjuvant hormone therapy (AHT).

The study comprised 1,292 patients with locally advanced adenocarcinoma of the prostate and a minimum of 15% lymph node involvement. There were four treatment arms: WPRT+NHT, WPRT+AHT, PORT+NHT, and PORT+AHT. This study revealed no statistically significant differences in overall survival; the only trend towards an improvement in progression-free survival was observed in the WPRT+NHT arm compared with the PORT+NHT and WPRT+AHT arms. There seems to have been an unexpected interaction between the timing of the hormone therapy and the scope of the radiation therapy.

Lawton *et al.* recommended further studies to find out whether this failure to demonstrate

a significant advantage for WPRT+NHT compared with PORT+AHT is down to chance, or whether there is a biological explanation.

Original article Lawton CA *et al.* (2007) An update of the phase III trial comparing whole pelvic to prostate only radiotherapy and neoadjuvant to adjuvant total androgen suppression: updated analysis of RTOG 94-13, with emphasis on unexpected hormone/radiation interactions. *Int J Radiat Oncol Biol Phys* **69**: 646–655

Development of imatinib-resistant clones in metastatic GISTs

Gastrointestinal stromal tumors (GISTs) usually develop as a result of mutations in the gene that encodes stem cell factor receptor tyrosine kinase (KIT). Imatinib, a selective inhibitor of KIT and other tyrosine kinases, is the first-line therapy for metastatic and unresectable malignant GISTs but in some patients disease progression occurs despite continued imatinib therapy. Desai *et al.* previously noted novel imaging patterns in the tumors of patients with GISTs and decided to assess radiologic patterns of GIST progression to determine the factors that underlie relapse during imatinib therapy.

Disease progression was monitored with CT, PET and MRI imaging in 89 patients with metastatic GISTs treated with imatinib. During 43 months of follow-up, progressive disease occurred in 48 patients, 23 of whom showed a unique 'nodule' pattern of progression. Imatinib resistance developed within the original tumor mass in 5 of the 23 patients who showed nodule-type progression. The average survival time for patients with nodular disease progression was 35.1 months, versus 44.6 months for patients whose tumors progressed without nodules. Biopsies revealed new activating kinase mutations in 8 out of 10 patients with this new pattern of 'nodule within a tumor' progression.

The authors conclude that the 'nodules' represent the emergence of imatinib-resistant clones in the original tumor, a pattern of disease progression not previously detected in patients with solid tumors, and a novel observation that seems to be a paradigm in GISTs. They recommend that this type of drug-resistant nodule should be classified as a new lesion and should be regarded as partial progression of GISTs.

Original article Desai J *et al.* (2007) Clonal evolution of resistance to imatinib in patients with metastatic gastrointestinal stromal tumors. *Clin Cancer Res* **13:** 5398–5405